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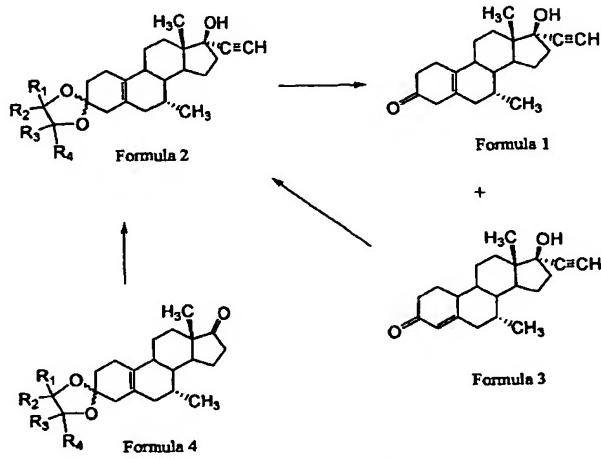
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- m.15, PL-03-980 Warszawa (PL). WOJCIECHOWSKA, Wanda [PL/PL]; ul. Kobuza 17, PL-02-841 Warszawa (PL). FITAK, Hanna [PL/PL]; Al. Reymonta 23 m.261, PL-01-840 Warszawa (PL).
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[Continued on next page]

(54) Title: PROCESS AND INTERMEDIATES TO PREPARE 17.BETA.-HYDROXY-7.ALFA.-METHYL-19-NOR-17.ALFA.-PREGN-5(10)-EN-20-YN-3-ONE



(57) Abstract: The present invention is a process for the preparation of 17 β -hydroxy-7 α -methyl-19-nor-17 α -pregn-5(10)-en-20-yn-3-one (17 α -ethynyl-17 β -hydroxy-7 α -methyl-5(10)-estren-3-one, tibolone) of formula 1, which comprises hydrolysis of 17 α -ethynyl-17 β -hydroxy-7 α -methyl-5(10)-estrene 3,3-cyclic ketals of formula 2, where groups R₁, R₂, R₃ and R₄ are hydrogen atoms or alkyl groups, or R₁ and R₃, taken together with the carbon atoms within the dioxolane ring to which they are attached, form an alicyclic ring fused to the dioxolane ring, with R₂ and R₄ being hydrogen atoms, or R₁ and R₃ together with the carbon atoms to which they are attached form an aromatic ring fused to the dioxolane ring, where R₂ and R₄, taken together, form a chemical bond within said aromatic ring. In addition, the present invention includes an intermediate, compound of formula 2 and two processes to prepare 17 α -ethynyl-17 β -hydroxy-7 α -methyl-5(10)-estrene 3,3-cyclic ketals of formula 2: (a) by contacting 17 α -ethynyl-17 β -hydroxy-7 α -methyl-4-estren-3-one with vicinal diols in the presence of a protic acid, and (b) by contacting 7 α -methyl-5(10)-estrene-17-one 3,3-cyclic ketals of formula 4, where R₁-R₄ are defined as above, with metal acetylides, in inert solvents.



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B. FIELDS SEARCHED

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C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DINUNNO, CECIL M. ET AL: "7.alpha.-Methylnorethindrone enanthate 10.beta.-hydroperoxide: isolation and characterization" STEROIDS (1983), 42(4), 401-8 , XP009027390 page 404, line 10-21 compound III page 406, paragraphs 2,3 --- -/-</p>	17-20

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HOYTE, ROBERT M. ET AL: "7.alpha.-Methyl-17.alpha.-(E-2'-125I!odo vinyl)-19-nortestosterone: a new radioligand for the detection of androgen receptor" STEROIDS, vol. 58, no. 1, 1993, pages 13-23, XP009027391 page 15, column 1, paragraph 1; figure 1	17-20
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X	US 4 308 265 A (BLYE RICHARD ET AL) 29 December 1981 (1981-12-29) cited in the application	17, 18
Y	column 2, line 65 -column 3, line 13; example 3	1-8, 12-16, 21-23
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Y	VAN VLIET N P ET AL: "An alternative synthesis of 17.beta.-hydroxy-7.alpha.-methyl-19-nor -17.alpha.-pregn-5(10)-en-20-yn-3-one (Org OD 14)" RECUEIL DES TRAVAUX CHIMIQUES DES PAYS-BAS, ELSEVIER SCIENCE PUBLISHERS. AMSTERDAM, NL, vol. 105, no. 4, April 1986 (1986-04), pages 111-115, XP002099865 ISSN: 0165-0513 cited in the application Scheme 2, compounds 4, 13 and 21 page 115, column 1, paragraph 3 -page 115, column 2, paragraph 1	1-8, 12-16, 21-23
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